REMARKS

This amendment is responsive to the Office Action of March 30, 2009. Reconsideration and allowance of claims 1-18, 22, 23, and 25-30 are requested.

Claims 1-13, 15-18, 22, 23, and 25-30 are pending in this application.

Claims 14 and 24 have been cancelled.

Claims 2-4 stand withdrawn.

The Office Action

Claims 1, 5-13, 15-18, and 22-30 were rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 7,252,720 to Foster, *Ernst and Race* (1993), and U.S. Patent Application Serial No. 10/467,591 to Kritzler (U.S. Pub. No. 2004/0106188).

The Present Application

Prions are resistant to many conventional treatment processes used for destruction of microorganisms. Their behavior also differs in many cases to that of conventional proteins. In particular, conformational changes in the structure of prions in various treatments results in a β-sheet structure which is highly resistant to degradation.

The present inventors have found that a treatment in which one or more non-halogenated phenols are combined with an inorganic salt, e.g., sodium chloride, can inactivate prions on a body.

The References of Record

The Foster reference discloses a method for removing contamination from ion-exchange chromatography columns. Foster uses sodium chloride solution to elute and remove prions from the column (col. 3, lines 41-44) through a type of ion exchange mechanism (col. 4, lines 31-33). The prions are not destroyed. Specifically, Foster notes that material eluted during the first 2M sodium chloride wash was subsequently found to have high prion infectivity (col. 6, lines 9-30), suggesting that little or no conformational change has occurred. There is no mention of using phenols to elute the prions.

The Ernst and Race reference discloses treating a scrapie-infected hamster brain homogenate with LpH. As mentioned in the Ernst and Race article, LpH is an aqueous acid phenolic disinfectant which contains a halogenated phenol, o-benzyl-p-chlorophenol at 6.1%, as well as non-halogenated phenols.

Kritzler, et al. discloses methods for treating a surface suspension or solution contaminated with prion protein with enzymes. In paragraph 41, Kritzler discloses that certain surfactants tend to bind to proteins and initiate unfolding of their tertiary structure. In paragraph 42, it is noted that inorganic salts can induce conformational transitions in proteins. These paragraphs detail the understanding about proteins in general and not about prion proteinaceous material. It can be seen from Table 1 that these general assumptions do not apply to prions (as represented by models of proteins such as bovine albumin with high globulin content).

The Claims Distinguish Patentably Over the References of Record

Claim 1 has been amended to recite a method of treating a body which is contaminated with infectious prions. The method includes contacting the body with a composition comprising a phenol and a soluble inorganic salt, to effect a change in the three dimensional structure of the prion protein and inactivate prions on the body. The phenol in the composition consists solely of non-halogenated phenol.

Support for the amendments to claim 1 are to be found in the specification at page 10, last paragraph.

The references cited, alone or in combination, do not suggest such a method.

The **Foster** reference discloses a method for removing contamination from ion-exchange chromatography columns. Foster uses a sodium chloride solution to elute and remove prions from the column (col. 3, lines 41-44) through a type of ion exchange mechanism (col. 4, lines 31-33). As the Examiner acknowledges, this reference does not teach the use of a phenol. Foster also suggests that the method may be used in cleaning surgical instruments. However, Foster provides no basis for expecting the method which is workable on chromatographic columns to metal surfaces which do not work by ion exchange.

Specifically, Foster notes that material eluted during the first 2M sodium chloride wash was subsequently found to have high prion infectivity (col. 6, lines 9-30). One of ordinary skill in the art would therefore understand from Foster that Kritzler's suggestion that salts can introduce conformational transitions in proteins is not applicable to prions. Further, Foster uses the salt solution for washing the substrate. There is no suggestion that salt be combined with a prion deactivation composition. Rather, Foster suggests that prion deactivation with an alkali should follow (or alternate with) the salt treatment step. See claim 6 and col. 4, lines 23-30. Thus, Foster teaches against using salt in combination with a prion deactivation composition.

Ernst & Race (1993) discloses treating a scrapie-infected hamster brain homogenate with LpH. There is no suggestion in this reference that the composition include a soluble inorganic salt. Ernst & Race purports LpH to be a complete solution to the scrapie infection problem and provides no motivation or reason to incorporate an inorganic salt. Moreover, the LpH used by Ernst and Race employs a halogenated phenol as a primary ingredient (6.4% *o*-benzyl-*p*-chlorophenol). Ernst and Race make no suggestion that the composition would be effective against prions without the halogenated phenol and indeed in later work, advise against using compositions which lack *o*-benzyl-*p*-chlorophenol, such as LpH-SE (Race and Gregory, Inactivation of Transmissible Spongiform Encephalopathy (Prion) Agents by Environ LpH, J. Virol., pp. 2164-2165, Feb 2004).

The Examiner points to paragraphs 41 and 42 of **Kritzler, et al.** as disclosing that inorganic salts can induce conformational transitions in prion proteins. However, these sections refer to proteins in general. One of ordinary skill in the art would have no expectation that inorganic salts can induce conformational changes in prions, particularly in light of Foster, which clearly demonstrates that they do not. Moreover, while most proteins have a hydrophilic character, prions are highly hydrophobic, which would lead one of ordinary skill in the art to expect differences in behavior to conventional proteins.

Accordingly, it is submitted that the Examiner has not met the burden, under §103(a), of establishing a *prima facie* case of obviousness. Moreover, it is

submitted that the references alone or in combination, do not suggest a method for the treatment of a body which is contaminated with prions, which includes contacting a body with a composition comprising a non-halogenated phenol and a soluble inorganic salt, such as sodium chloride, to effect a change in the three dimensional structure of the prion protein and inactivate prions on the body.

The present inventors have found that an inorganic salt, used in combination with one or more non-halogenated phenols, improves the effectiveness of the phenol, especially at low pH. This is believed to be due, at least in part, to the effects on the phenol solubility. This is not taught or suggested by the references.

Accordingly, it is submitted that claim 1, and claims 5-9, 15, 16, 18, 22, and 25-28 dependent therefrom, are patentable over the cited references.

Claim 11 calls for a method of treating a medical device which is contaminated with infective prions which includes contacting the device with a composition comprising a non-halogenated phenol and a soluble inorganic salt to inactivate prions on the device, the soluble inorganic salt including sodium chloride. The phenol in the composition consists solely of non-halogenated phenol.

Support for the amendments to claim 11 are to be found in the specification at page 10, last paragraph.

The references of record do not suggest such a method. The salt treatment method taught by Foster does not destroy prions. Ernst and Race make no suggestion that a non-halogenated phenol would be improved by addition of sodium chloride. The LpH formulation includes o-benzyl-p-chlorophenol, a halogenated phenol. As shown by the Race and Raymond article, LpH-SE, which has no halogenated phenol, is shown to be much less effective. Foster teaches that salt has no effect on the infectivity of prions. Further, while Foster suggests that the method may be used for cleaning substrates, such as surgical instruments, there is no suggestion that the salt solution would inactivate prions on the instruments. Moreover, there is no suggestion of using salt, other than as a wash. Foster teaches against combining salt with a prion deactivation treatment, such as an alkali. Rather, the alkali is used in separate steps.

Thus, the reference provides no motivation for combining a non-halogenated phenol with sodium chloride. Accordingly, it is submitted that claim 11, and claims 12 and 17 dependent therefrom, are patentable over the cited references.

Claim 13 calls for a method of treating a body which is contaminated with infective prions. The method includes contacting the body with a composition consisting of *o*-phenylphenol as the phenol in a solution that includes brine.

The references do not suggest such a method. None of the references, with the exception of Ernst and Race, suggests treatment with phenol that includes *o*-phenylphenol. Ernst and Race make no suggestion that the LpH composition would be effective without halogenated phenols, which are the predominant phenols in the LpH composition. Further, there is no suggestion in Ernst and Race that phenols, such as *o*-phenylphenol be used in combination with brine. Foster teaches that salt does not destroy infectivity and further teaches that it should not be used in combination with a prion decontamination treatment, such as alkali. Kritzler does not suggest that prions undergo conformational changes in the presence of brine nor suggest what a conformational change, if it were to occur, would have on prion infectivity. Kritzler indicates that inorganic salts have an effect on conformational changes in conventional proteins. However, as Foster demonstrates, this is not generalizable to prions, since the salt treatment of Foster was found to have no effect on prion infectivity. Thus, one of ordinary skill in the art would not expect brine to have any effect on the ability of a combination of *o*-phenylphenol and brine to inactivate infective prions.

Accordingly, it is submitted that claim 13 distinguishes patentably over the references of record.

Claim 23 calls for a method of treating a body which is contaminated with prions that includes contacting the body with a composition comprising at least one phenol, the composition comprising a phenol concentration of at least 0.005M and an inorganic salt which is present at a concentration of at least 2% by weight, the phenol including at least one of the group consisting of thymol; *p*-phenylphenol; 2,3-dimethylphenol; 3,5-dimethoxyphenol; 2,6-dimethoxyphenol; *o*-phenylphenol; *p*-tertiary-amylphenol; *o*-cresol; p-cresol; 3,4-dihydroxybenzoic acid; *p*-hydroxybenzoic

acid; caffeic acid; protocatechuic acid; *p*-nitrophenol; 3-phenolphenol; 2,3-dimethoxyphenol; and para-phenylphenol. The body is contacted with the composition to effect a log reduction of at least 4.1 for prions on the body.

The references of record do not suggest treating a body with one or more of the above-mentioned non-halogenated phenols and an inorganic salt at a concentration of at least 2%. The salt treatment method taught by Foster does not destroy prions. Nor is there any suggestion that Foster's salt wash be combined with a phenol. Rather, Foster teaches against combining the salt wash with a prion decontamination composition. Thus, there is no suggestion for use of sodium chloride in a phenol-based disinfectant, such as LpH, as taught by Ernst and Race. Nor is there any suggestion that the salts proposed by Foster would be useful as agents favoring unfolding in Kritzler's system. There is no suggestion in Foster that the prions undergo conformational unfolding in the process. Further, Ernst and Race make no suggestion that LpH would be active against prions without a halogenated phenol as its primary ingredient.

Accordingly, it is submitted that claim 23 distinguishes patentably and unobviously over the references of record.

Claim 29 calls for a method of treating a body which is contaminated with infectious prions. The method includes contacting the body with a composition to inactivate prions on the body. The composition includes a phenol, a cosolvent, water, and a surfactant selected from the group consisting of sulphonic acids, sulfonates, and combinations thereof. The phenol in the composition consists solely of non-halogenated phenol.

In paragraph 0041, Kritzler discloses that certain surfactants tend to bind to proteins and initiate unfolding of their tertiary structure. This paragraph, however, details the understanding about proteins in general and not about prion proteins. There is no suggestion that detergents affect conformational change in prions or have any effect on the infectivity. Note in particular, the Darbord reference, which indicates that detergents are ineffective against prions.

Nor is there any suggestion that surfactants should be used in combination with phenols, specifically, non-halogenated phenols. As shown by Foster, the

behavior of prions is not predictable. Foster shows that salts do not induce conformational changes in prions, thus there is no reason for expecting that surfactants would do so either. Ernst and Race do not suggest that LpH would be effective without halogenated phenol as the primary ingredient. Thus, one of ordinary skill in the art would have no expectation of success in combining a surfactant selected from the group consisting of sulphonic acids and sulfonates with a non-halogenated phenol.

Thus, it would not have been obvious, in view of the cited references, to contact a body with a composition which includes a non-halogenated phenol, a cosolvent, water, and a surfactant selected from the group consisting of sulphonic acids, sulfonates, and combinations thereof.

Accordingly, it is submitted that claim 29, and claim 10 dependent therefrom, distinguish over the references of record.

Claim 30 calls for a method of treating a body which is contaminated with infectious prions. The method includes contacting the body with a composition to inactivate prions on the body, the composition consisting of a non-halogenated phenol comprising *o*-phenylphenol, a cosolvent, sodium chloride, water, and a surfactant, the composition effecting a change in the three dimensional structure of the prion protein and inactivating prions on the body.

Support for the amendments claim 30 are to be found at page 10, last paragraph of the specification and in Table 1.

The references of record do not suggest treating a body with a composition as claimed.

Accordingly, it is submitted that claim 30 distinguishes over the references of record.

CONCLUSION

For the reasons set forth above, it is submitted that claims 1-13, 15-18 and 22, 23, and 25-30 (all pending claims) distinguish patentably over the references of record and meet all statutory requirements. An early allowance of all claims is requested.

☒ Remaining Claims, as delineated below:

(1) FOR	(2) CLAIMS REMAINING AFTER AMENDMENT LESS HIGHEST NUMBER PREVIOUSLY PAID FOR		(3) NUMBER EXTRA
TOTAL CLAIMS	**25**	**27**	**0**
INDEPENDENT CLAIMS	**6**	**6**	**0**

In the event the Examiner considers personal contact advantageous to the disposition of this case, she is requested to telephone the undersigned at (216) 363-9000.

Respectfully submitted,

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